Intrinsic and method-induced variation of the bleeding time and related parameters

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Download date: 15 Sep. 2023
Sex-Related Difference in Plasma von Willebrand Factor (vWF:Ag and vWF:RiCof) Levels in Adolescents

Dear Sir,

Von Willebrand disease (vWD) is probably the most frequent hereditary disorder of haemostasis. The diagnosis of type I vWD is still based on the demonstration of decreased plasma levels and ristocetin cofactor activity of von Willebrand factor (vWF). Accordingly, the definition of the lower normal limits of these measurements in different populations is essential for the diagnosis, specially in individuals with the mild form of the disease. It is known that the concentration of plasma vWF is positively correlated with age, is higher in children in the age range 11-14 years, and is higher in individuals of blood type A, B and AB than in those of type O. The sex of the individual has not been shown to influence the levels of plasma vWF (1).

The aim of this study was to define the normal range of plasma vWF in school age children and adolescents, the age cohort most often derived to our laboratory for diagnostic assessment of muco-cutaneous

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References

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the bloodstream from the bleeding time wound and a standardized bleeding time wound does not significantly improve the situation.

The bleeding time values we measured lead to 95% confidence limits for individual measurements that are large, and do not deviate much from what has been reported earlier (3, 6). The variabilities of the other three parameters we investigated appear to be worse than the bleeding time. The intra-individual variability, a property that has hardly been investigated in the past seems to do no better. We conclude that there possibly is an intrinsically lower limit to the variability of this test that can hardly be influenced by instrumental sophistication and that current tests may be not far off this limit.

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**Thrombosis during Pregnancy and Surgery in Patients with Congenital Deficiency of Antithrombin III, Protein C, Protein S**

Sir,

Association of a risk situation with about 50% of thromboses in patients with inherited thrombophilia is well established (1-4); on the other hand, prevalence of thrombosis during risk situations in such patients has been seldom analyzed (4-6). Conard et al. (5) reported a thrombotic complication in 19% of pregnancies in PC-deficiency and in 11% of pregnancies in PS-deficiency, at significant variance with prevalence of thrombosis during pregnancy and post-partum in AT III-deficiency (44%). In other series of PC-deficient women pregnancy was complicated by thrombosis in 16-17% of the cases (4, 6). Venous thromboembolism in patients undergoing surgery without prophylaxis was estimated 17% in AT III-deficiency (7) and 10% in PC-deficiency (4).

We analyzed the medical records of 238 individuals (M/F 121/117) with inherited thrombophilia (AT III = 94, PC = 103, PS = 41) belonging to 73 different kindreds (AT III = 26, PC = 34, PS = 13): 129 (54%) had previously suffered thrombosis and 62 have had recurrent episodes. In 83 of 168 major venous thrombotic episodes (49%) a triggering cause was recognized; the most frequent were pregnancy and puerperium (30 cases, 17%) and surgery (21 cases, 12%). Overall, thrombosis following a risk event was more frequent in AT III-deficiency (36/80, 45%) than in PC-deficiency (20/88, 22%, X^2 = 9.35, p <0.005) or PS-deficiency (13/56, 23%, X^2 = 6.78, p <0.01).

A total of 121 pregnancies without prophylaxis was recorded in 58 women. Thrombosis complicated 37% of pregnancies and deliveries in AT III-deficiency (20/54), at significant variance with PC-deficiency (6/48, 12%, X^2 = 8.05, p <0.005) and PS-deficiency (3/22, 13%, X^2 = 4.05, p <0.05) (Table 1); most of the thromboses occurred during the post-partum (21/28, 75%), whatever the type of deficiency (AT III = 13/19; PC = 5/6; PS = 3/3). The prevalence of thrombosis during pregnancy as compared to postpartum (considering of post-partum only the cases without antithrombotic treatment) was statistically different in AT III-deficiency (6/52 pregnancies, 11%, vs 13/44 post-partum periods, 29%, X^2 = 4.86, p <0.05) but not in PC-deficiency (1/48, 2%, vs 5/47, 10%, X^2 = 2.93, p <0.1) and PS-deficiency (0/22 vs 3/22, 13%, X^2 = 0.92, p = 0.34).

### Table 1 Development of thrombotic complications during pregnancies without prophylaxis

<table>
<thead>
<tr>
<th>Patients</th>
<th>AT III</th>
<th>PC</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patiens</td>
<td>24</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Pregnancies</td>
<td>51</td>
<td>48</td>
<td>22</td>
</tr>
<tr>
<td>Abortions</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients with thrombosis</td>
<td>16</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Pregnancies with thrombosis</td>
<td>20</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

### Table 2 Surgical interventions (without prophylaxis) recorded in 78 patients. Between brackets the thrombotic complications observed in 33 patients

<table>
<thead>
<tr>
<th>Patients</th>
<th>AT III</th>
<th>PC</th>
<th>PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>31</td>
<td>28</td>
<td>19</td>
</tr>
<tr>
<td>Abdominal surgery</td>
<td>23 (6)</td>
<td>12 (2)</td>
<td>17 (3)</td>
</tr>
<tr>
<td>Urologic surgery</td>
<td>2 (1)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Gynecologic surgery</td>
<td>3</td>
<td>5 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
<td>5 (2)</td>
<td>5 (4)</td>
<td>1</td>
</tr>
<tr>
<td>Other interventions</td>
<td>4</td>
<td>2</td>
<td>7</td>
</tr>
</tbody>
</table>

### Table 3 Thrombosis in: AT III, PC-PS, X^2, p

<table>
<thead>
<tr>
<th>Patients</th>
<th>AT III</th>
<th>PC-PS</th>
<th>X^2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal surgery</td>
<td>6/23 (26%)</td>
<td>5/29 (17%)</td>
<td>0.60</td>
<td>&lt;0.50</td>
</tr>
<tr>
<td>High-risk surgery</td>
<td>3/10 (30%)</td>
<td>6/14 (43%)</td>
<td>0.41</td>
<td>&lt;0.60</td>
</tr>
<tr>
<td>All interventions</td>
<td>9/37 (24%)</td>
<td>11/52 (21%)</td>
<td>0.08</td>
<td>&lt;0.80</td>
</tr>
</tbody>
</table>

References


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